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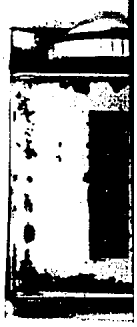

USSR MONOGRAPH ON THE TOXICITY OF THE INFLUENZA VIRUS

[Comment: The following is a review of L. Ya. Zakstel'skaya's monograph Toksichnost' Virusa Grippa (Toxicity of the Virus of Influenza), published by the Academy of Medical Sciences USSR, Moscow, 1953, 84 pages. This review, written by G. N. Chistovich, was published in Zhurnal Mikrobiologii, Epidemiologii, i Immunobiologii, No 7, Moscow, July 1954, pages 113-114.]

The book being reviewed is a candidate's dissertation which has been revised to some extent. This dissertation has been carried out at the Institute of Virology, Academy of Medical Sciences USSR, under the direction of Prof V. D. Solov'yev. It deals with the clarification of one of the most important aspects of the pathogenic activity of the influenza virus.

In the introduction the author points out that the explanation of the pathogenesis of influenza solely by the spontaneous reproduction of the virus protein during the process of infection cannot be regarded as satisfactory. A brief review of the literature dealing with the character and significance of toxic phenomena in influenza follows. After this the author goes on to describe her own experimental, clinical, and laboratory observations, which are of great interest both for specialists in the field of microbiology and for clinicists.

First of all, the author established that allantois cultures of the virus of influenza or suspensions of infected lungs, after being introduced in large doses into a vein or into the brain of white mice, bring about the death of the animals within 15-48 hours. The disease produced differs radically from an ordinary experimental influenza infection. It is not connected with the multiplication of the virus and is characterized by clinical and pathological phenomena typical for an acute toxicosis. The author further shows that introduction of large doses of the virus into the anterior occular chamber of rabbits or guinea pigs results in the development of a toxic keratitis. Finally, the toxic action of the influenza virus can be detected in vitro with the aid of Tarusov's striction method.

The degree of toxicity of allantois cultures and of lung suspensions corresponds to the quantity of the virus contained in them. Heating, irradiation with sunlight or ultraviolet light, treatment of the material containing the virus with formalin, adsorption on erythrocytes, or centrifuging leads to simultaneous changes in the infectious properties and the toxicity. Anti-influenza immune sera and sera of patients recovering from influenza neutralize completely the toxic activity of the virus. This neutralization has a type-specific character and in some cases is specific even for individual strains of the virus.

White mice which have been exposed to the toxic action of moderate doses of the virus, or have been subjected to artificial immunization, become protected both against infection and intoxication with the influenza virus. Using a large number of experimental animals, the author investigated step by step the development of the resistance to infection and intoxication after a single introduction of a small dose of the virus into the peritoneal cavity. It has been shown in the experiments described that the antitoxic protection reaches the highest level as early as on the 9-11th day. It remains on this

level until the 30th day and then drops gradually. Corresponding changes are observed in the resistance to infection, the level of sensitivity of the tissues to the toxic action of the virus in striction tests, and the titer of antihemagglutinins in the blood. The author arrives at the conclustion that the antitoxic immunity acquired in the process of protective inoculation is closely connected with a modification of the reactivity of the tissues of the animal and an accumulation of specific antibodies in the serum. However, she also emphasizes the role played by changes in the general reactivity of the organism.

After setting herself the task of establishing the presence of a specific poison in the organism of influenza patients and of clarifying its significance in the pathogenesis of the disease, Zakstel'skaya demonstrates that the blood of mice which have recovered from an influenza pneumonia acquires a considerable toxicity. She then discusses the clinical and laboratory investigation carried out on a group of 196 patients and finds that in the first hours and days of the disease, the blood of many of them is toxic and contains the influenza antigen. Following this, the toxicity rapidly drops if the pathogenic process takes a benignant course, and the level of antibodies rises parallel to the reduction of toxicity.

Zakstel'skaya makes the assumption that the effect on the organism of toxic substances originating from the causative factor of the disease suppresses the activity of the nervous system and brings about disturbances in the activity of the cardiovascular system (page 53).

In the next chapter, the possibility of using the toxic properties for the characterization of individual strains of the influenza virus and for the investigation of the processes of their adaptive modification is discussed.

The use of the toxicity test in the investigation of the immunogenicity of influenza vaccines appears very promising because of the possibility of exact dosage and of the short incubation period which enables one to shorten the time of the test. Furthermore, the author points out the possibility of using the toxinometric method of Tarusov for diagnostic purposes in human influenza.

In the final subdivision of the book, the results of investigations made hitherto are summarized and the line to be followed by future investigations is indicated. Specifically, the author points out that the occurrence of the influenza toxin is apparently closely connected with the presence of the virus particle and that attempts to isolate the toxin, as bacterial toxins have been isolated, has not succeeded hitherto. Toxic afflictions of the capillary circulation found in experimental work on poisoned animals show a great similarity with the changes observed in sick persons. The mechanism of the development of the disturbances in question is not clear as yet. It is possible that pathological reflexes take place which originate as a result of the harmful effect exerted by the toxin on the regulatory functions of the central nervous system. The fact that an antitoxic immunity develops in influenza makes the application of a specific serum therapy very promising.

The book ends with the conclusion that the capacity of the causative factor of influenza to exert a toxic action, which has been established in experiments, explains the development of neuroregulatory disturbances in this

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infection and makes it possible to investigate its pathogenesis from the standpoint of Pavlovian physiology. The bibliography which is appended to the book lists 137 source references in the Russian language and 10 foreign references.

On the whole, this monograph gives a lucid discussion of the problem and is of interest for that reason. The clarity of the exposition and the convincing nature of the experimental proofs increase its value.

However, some of the statements made by the author must be criticized. For instance, the conclusion that antitoxic immunity in a considerable measure depends on the presence of antibodies at the site where the toxin has been introduced or where it has formed (page 48) has not been adequately substantiated. It is not clear why the toxic properties of the serum of patients who have influenza are neutrialized by antiserums only on the first to second day of the disease, and cannot be rendered harmless in later attempts at neutralization (page 53). The discussion in regard to the adaptive character of the toxicity of the virus is not quite convincing (pages 60-61). According to an idea expressed by the author, strains which are pathogenic to human beings but do not induce upon isolation a lethal pneumonia in mice, must be toxic only to human beings but not to mice. However, the author does not cite any experimental data which support this hypothesis. The statement that the virus acquires both pathogenicity and toxicity in the process of its fight with the protective forces of the host organism (page 61) seems to be too abstract. It would have been better not to draw an analogy with rickettsiae (page 68), because data are available which indicate that it is possible to isolate and purify rickettsial toxins.

The editors (Leytes and Rotermel') share the author's responsibility for a number of shortcomings that are apparent in the book. One of the shortcomings consists in the use of inept foreign terms such as anesoinophilia, consolidation of the lungs, partial extravasation, virus-neutralizins, polystrainness etc. The expressions "lethal-toxic", "infectious-lethal," "reactive-toxic," "toxic-lethal," and "toxic-mortal" as applied to doses of the virus occur in the book. The book is also not improved by expressions such as "burying the virus" or "pathogenetic hemorrhages," and references to "virological (sic!) and physiological methods developed by I. P. Pavlov" (page 11), or to "microbes which are close to the viruses of mooseri orientalis rickettsiae" (page 12), or to "an evaluation of the immunogenicity of vaccines for diagnostic purposes" (page 63). In many places the punctuation used in the book conflicts with the rules of grammar.

There are also shortcomings in the bibliographic index: e.g., some authors whose work is quoted on pages 6, 8, and 9 are not named; the initials of Ye. B. Ginzburg are wrong; occasionally the alphabetic order is not observed; a publication by Kurashvili is listed twice; there are bad errors in the spelling of titles of foreign publications.

The reproduction of photographs on pages 18-20 leaves much to be desired. Furthermore, the captions in Figure 16 have been mixed up and the graph contradicts the text. Notwithstanding the many shortcomings indicated, the content of the monograph is worthy of praise, although the errors which have been made spoil the impression to that effect.

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One may express the hope that the publishers will be more exacting as far as the standards applied to the books produced by them are concerned. There is also a delay in publishing the monograph: although Zaktel'skaya's dissertation was defended in 1950, it became available to the readers only in 1953, i.e., 2 1/2 years later.

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